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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/685,403	10/10/2000	Peter R. Beetham	[illegible]	8644

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EXAMINER
KRUSE, DAVID H

ART UNIT	PAPER NUMBER
2638	

DATE MAILED: 02/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
09/685,403	BEETHAM ET AL.
Examiner	**Art Unit**
David H Kruse	1638

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

[illegible] to claim priority under 35 U.S.C. §§ 120 and/or 121

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ [illegible]

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-23 in Paper No. 10, filed 4 December 2001 is acknowledged. The traversal is on the ground(s) that to search and examine the claims of all the Groups together would not be a serious burden. This is not found persuasive because the protein of Group II is unrelated to the non-transgenic plant of Group I because they are structurally, functionally and compositionally distinct, and the protein of Group II cannot be used in the method of Group I.

The requirement is still deemed proper and is therefore made FINAL.

2. Claim 24 is withdrawn from further consideration pursuant to 37 CFR § 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR § 1.48(b) and by the fee required under 37 CFR § 1.17(i).

4. This application contains claim 24 drawn to an invention nonelected with traverse in Paper No. 10. A complete reply to the final rejection must include cancellation of

Information Disclosure Statement

5. The information disclosure statement filed 8 June 2001 has been considered with the following exceptions.

References AX on page 1 and BH on page 2 have not been considered because there is no clear relevance to the instant invention. Reference BI on page 2 has not been considered because Applicant has not supplied a translation from the German language of the reference for the Examiner's consideration or a brief statement of the relevance of this reference.

In addition, pending U.S. Patent application references AY-BC on page 1 have been considered, but are not deemed proper references for printing on the face of the issued patent. If a pending U.S. Patent application has issued, the Patent No. should be listed. Applicant's attention is directed to MPEP § 609 III.C(2) and III.C(3).

Drawings

6. The Draftsman has objected to the drawings as originally submitted. See PTO-948 attached.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. Correction of Informalities -- 37 CFR § 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability."

Addressed to the Official Draftsperson

2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR § 1.85(a). Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

8. Claims 1-13 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter.

The instant claims read on a naturally occurring mutant plant comprising a mutant EPSPS gene product. There is no evidence in the specification or the art that the specific mutations at claims 5-13 would not occur naturally. It is suggested that the claims be amended to read -- A(The) modified, non-transgenic plant -- to obviate this rejection.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

10. Claims 14-22 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claims 14 and 15 are rejected under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is: regenerating a non-transgenic herbicide resistant or tolerant plant from said plant cell.

12. Claims 20-22 recite the limitation "The plant according to claim 19" in line 1. There is insufficient antecedent basis for this limitation in the claim because said claims are further limiting a mutant EPSPS gene at claim 19, which is drawn to a method.

13. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 1-23 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant claims a method for producing a non-transgenic herbicide resistant or tolerant plant comprising introducing to a plant cell a recombinagenic oligonucleobase to produce a mutant EPSPS gene and a plant produced thereby.

[illegible] EPSPS protein by introducing an *Arabidopsis* gene encoding a wild-type

EPSPS protein into *Salmonella typhi* and introducing a recombinagenic oligonucleobase into the bacterium cell to produce a mutant EPSPS gene (see 6.1.5 on page 22 of the specification).

Applicant does not teach the claimed method in a plant or a herbicide resistant or tolerant plant produced thereby. The results at 6.2 on page 23, paragraph 2, are unclear as to whether the procedure was applied in *Arabidopsis* or if the modified EPSPS gene produced in the bacterium was introduced by transgenic means into the *Arabidopsis* plant and that said plant was herbicide resistant or tolerant.

In re Wands, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988) lists eight considerations for determining whether or not undue experimentation would be necessary to practice an invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

Applicant has not provided a working example of the claimed method in plants. The state of the art at the time of Applicant's invention was such that the claimed method had not been proven in introducing point mutations *in vivo* into a plant genome in a predictable manner. The nature of the invention is such that extensive guidance would have been required in terms of what recombinagenic oligonucleobases to use for

claimed method can be highly unpredictable as to what actual mutation would be

introduced into a target site and suggests that predictability can be highly site specific. The claim 4 method has proven to be far less predictable when used in plants than when the same method is used in mammalian cells, for example (Zhu *et al* 1999, PNAS-USA 96:8768-8773, see Table 2 on page 8771, and page 8772, right column, paragraph 2)(Rice *et al* 2000, Plant Physiology 123:427-437, see the Abstract on page 427). Because of the absence of working examples, state of the art, nature of the invention and unpredictability of the art, it would have required undue trial and error experimentation by one of skill in the art at the time of Applicant's invention to design a myriad of recombinagenic oligonucleobases to modify an EPSPS gene at all codons along the coding region, or even the specific sites claimed, and modify a myriad of plants to determine which combination would be operable in producing a non-transgenic herbicide resistant or tolerant plant comprising a mutant EPSPS gene, as broadly claimed.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Hawkes discloses a method of *in vivo* modification of a plant EPSPS encoding gene, using a recombinagenic oligonucleobase (see Example 4 on pages 18 and 19), by converting the codon encoding Thr_{174} to Ile, Pro_{178} to Ser and/or Gly_{173} to Ala as shown in SEQ ID NO: 2 (*Brassica napus*) (claim 14 and 16) and plant produced therefrom (claim 18). Hence, all of the claim limitations have been previously disclosed by Hawkes.

Claim Rejections - 35 USC § 102/103

17. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claims 1-13 and 20-23 are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Lebrun *et al* (WO 97/04103).

Lebrun discloses a non-transgenic Black Mexican Sweet Corn comprising a mutant EPSPS gene wherein an Ile has been substituted for the naturally occurring Thr_{102} and a Ser has been substituted for the naturally occurring Pro_{106}, said mutant EPSPS gene confers upon said corn plant resistance to glyphosate (see entire reference and SEQ ID NO: 4). Hence, Lebrun has previously disclosed all of the claim limitations

Sweet Corn, herbicide resistant, plant cell was *in vitro* or in a plant.

If Lebrun has only disclosed a glyphosate herbicide resistant cell line comprising a mutant EPSPS gene wherein an Ile has been substituted for the naturally occurring Thr_{102} and a Ser has been substituted for the naturally occurring Pro_{106}, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention to regenerate a glyphosate resistant corn plant from such a cell. Regeneration of corn from cultured cells was standard practice in the art at the time of Applicant's invention, thus one of skill would have had a reasonable expectation of success in regenerating a glyphosate herbicide resistant corn plant.

19. See *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985), which teaches that a product-by-process claim may be properly rejectable over prior art teaching the same product produced by a different process, if the process of making the product fails to distinguish the two products. In the instant case, the plants produced by the claimed process would not be distinguishable from naturally occurring mutant plants comprising a mutated EPSPS gene, plants produced by *in vitro* mutagenesis methods using chemicals or selection pressure in culture, or by any other *in vivo*-site directed mutagenesis methods in plants.

20. Claims 1 -23 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kmiec (U.S. Patent 5,756,325), filing date September 9, 1996, in view of Lebrun *et al* (WO 97/04103).

Kmiec teaches a method of introducing within a eukaryotic cell a predetermined

polynucleotide that encodes two regions homologous with a target sequence and a

heterologous region encoding the alteration (Claims 24 and 30, and columns 7, 8 and 13). The method of Kmiec introduces the alteration into the target genome using a recombinagenic oligonucleobase via the cellular recombination/repair mechanisms (column 4, second paragraph).

Kmiec does not specifically teach said method within a plant cell to produce a mutant EPSPS gene. Kmiec does suggest use of the method in plant cells at claim 26 and 33.

The teachings of Lebrun are discussed above, specifically a mutant EPSPS gene wherein an Ile has been substituted for the naturally occurring Thr_{102} and a Ser has been substituted for the naturally occurring Pro_{106}, said mutant EPSPS gene confers upon said corn plant resistance to glyphosate.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of Kmiec using the teachings of Lebrun to modify *in vivo* the EPSPS gene of a plant to produce a plant resistant to glyphosate herbicide. The success of Kmiec in producing point mutations *in vivo* in other eukaryotic systems that are typically intransigeant to such methods would have given one of skill a reasonable expectation of success. The teachings of Lebrun would have directed one of skill in the art as to what exact changes in the coding region of an endogenous EPSPS gene should be modified to produce herbicide resistance in the modified plant.

Conclusion

21. No claims are allowed.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (703) 306-4539. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy Nelson can be reached at (703) 306-3218. The fax telephone number for this Group is (703) 872-9306 Before Final or (703) 872-9307 After Final.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Kim Davis whose telephone number is (703) 305-3015.

David H. Kruse, Ph.D.
7 February 2002